

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (Previously presented): A composition comprising chemically defined valency platform molecules, wherein the valency platform molecules individually comprise a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons, and wherein said valency platform molecules have a polydispersity less than 1.2.

Claim 2 (Previously presented): The composition of claim 1, wherein the valency platform molecules individually comprise a second high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons.

Claim 3 (Previously presented): The composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 22,000 Daltons.

Claim 4 (Previously presented): The composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 40,000 Daltons.

Claim 5 (Previously presented): The composition of claim 1, wherein the high molecular weight polyethylene oxide group has the formula:



wherein n is greater than about 500.

Claim 6 (Previously presented): The composition of claim 5, wherein n is greater than about 600.

Claim 7 (Previously presented): The composition of claim 5, wherein n is greater than about 700.

Claim 8 (Previously presented): The composition of claim 5, wherein n is greater than about 800.

Claim 9 (Previously presented): The composition of claim 1, wherein the valency platform molecules individually comprise a core group and at least three arms wherein each arm comprises a terminus.

Claim 10 (Previously presented): The composition of claim 9, wherein the core group comprises the high molecular weight polyethylene oxide group.

Claim 11 (Previously presented): The composition of claim 9, wherein an arm comprises the high molecular weight polyethylene oxide group.

Claim 12 (Previously presented): The composition of claim 9, wherein the high molecular weight polyethylene oxide group is attached to the core or one of said arms.

Claim 13 (Canceled)

Claim 14 (Previously presented): The composition of claim 1, wherein the valency platform molecules individually comprise at least three reactive conjugating groups selected from the group consisting of hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide, aldehyde, ketone, carboxylic acid halide, α -halocarbonyl, α,β -unsaturated

carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea, hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide, α,β -unsaturated sulfone, aminoxy, semicarbazide, and β -aminothiol.

Claim 15 (Previously presented): The composition of claim 1, wherein the valency platform molecules individually comprise at least 3 aminoxy groups.

Claim 16 (Previously presented): The composition of claim 1, wherein the valency platform molecules individually comprise at least 3 carbamate groups.

Claim 17 (Previously presented): A composition comprising conjugates comprising biologically active molecules and the valency platform molecules according to claim 1.

Claim 18 (Previously presented): The composition of claim 17, wherein the biologically active molecules are selected from the group consisting of polysaccharides, polypeptides, nucleic acids, and lipids.

Claim 19 (Previously presented): The composition of claim 17, wherein the conjugates are B cell toleragens.

Claim 20 (Currently amended): The composition of claim [[18]] 17, wherein the biologically active molecules comprise a nucleic acid or analog thereof, which specifically binds to an anti-double stranded DNA antibody.

Claim 21 (Previously presented): The composition of claim 19, wherein the biologically active molecules are β_2 GPI domain 1 polypeptides or analogs thereof that specifically bind to a β_2 GPI-dependent antiphospholipid antibody.

Claim 22 (Previously presented): The composition of claim 21, wherein the conjugates are effective for the treatment of antibody mediated thrombosis.

Claim 23 (Previously presented): The composition of claim 18, wherein the biologically active molecules are α Gal epitopes or analogs thereof that specifically bind to an anti- α Gal antibody.

Claim 24 (Previously presented): A pharmaceutically acceptable composition comprising the composition of claim 17 and a pharmaceutically acceptable carrier.

Claim 25 (Previously presented): A conjugate comprising a chemically defined valency platform molecule and a polypeptide comprising a β_2 GPI domain 1 polypeptide, wherein the conjugate comprises a high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Daltons.

Claim 26 (original): The conjugate of claim 25, wherein the valency platform molecule comprises at least 3 aminoxy groups.

Claim 27 (original): The conjugate of claim 25, wherein the valency platform molecule comprises at least 3 carbamate groups.

Claim 28 (Previously presented): The conjugate of claim 25, wherein the high molecular weight polyethylene oxide group has a molecular weight greater than about 22,000 Daltons.

Claim 29 (original): The conjugate of claim 25, wherein the valency platform molecule comprises a core group and at least three arms, wherein each arm comprises a terminus.

Claim 30 (original): The conjugate of claim 25, wherein the polypeptide specifically binds to a β_2 GPI-dependent antiphospholipid antibody.

Claim 31 (original): The conjugate of claim 30, wherein the polypeptide lacks a T cell epitope capable of activating T cells in an individual having β_2 GPI dependent antiphospholipid antibodies.

Claim 32 (original): The conjugate of claim 25, wherein the β_2 GPI domain 1 polypeptide comprises at least five contiguous amino acids of Figure 19 (SEQ ID NO: 2).

Claim 33 (original): The conjugate of claim 25, wherein the β_2 GPI domain 1 polypeptide comprises amino acids Nos. 2-63 of SEQ ID NO: 2.

Claim 34 (Previously presented): The conjugate of claim 25, wherein the conjugate is selected from the group consisting of compounds 200, 202, 203, and 205 shown in Figure 7 and compound 300 shown in Figure 16, wherein D1 in said structures is a polypeptide consisting of amino acids No. 2-63 of SEQ ID NO: 2.

Claim 35 (Previously presented): The composition of claim 23, wherein the biologically active molecules are said α Gal epitopes.

Claim 36 (Previously presented): The conjugate of claim 25, wherein the conjugate is effective for the treatment of antibody mediated thrombosis.

Claim 37 (Previously presented): The composition of claim 17, wherein the average total molecular weight of the conjugates is no greater than about 200,000 Daltons.

Claim 38 (Previously presented): The composition of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 22,000 Daltons.

Claim 39 (Previously presented): The composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 30,000 Daltons.

Claim 40 (Previously presented): The composition of claim 17, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 40,000 Daltons.

Claim 41 (Previously presented): The composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 50,000 Daltons.

Claim 42 (Previously presented): The composition of claim 1, wherein the high molecular weight polyethylene oxide group has a molecular weight of greater than about 100,000 Daltons.

Claim 43 (Previously presented): The composition of claim 17, wherein the high molecular weight polyethylene oxide group has the formula:



wherein n is greater than about 500.

Claim 44 (Previously presented): The composition of claim 43, wherein n is greater than about 600.

Claim 45 (Previously presented): The composition of claim 43, wherein n is greater than about 700.

Claim 46 (Previously presented): The composition of claim 43, wherein n is greater than about 800.

Claim 47 (Previously presented): The composition of claim 5, wherein n is greater than about 900.

Claim 48 (Previously presented): The composition of claim 5, wherein n is about 400 to 550.

Claim 49 (Previously presented): The composition of claim 5, wherein n is 520 to 600.

Claim 50 (Previously presented): The composition of claim 5, wherein n is 600 to 800.

Claim 51 (Previously presented): The composition of claim 5, wherein n is 600 to 1000.

Claim 52 (Previously presented): The composition of claim 17, wherein the valency platform molecules individually comprise a second high molecular weight polyethylene oxide group having a molecular weight of at least about 18,000 Da.

Claim 53 (Previously presented): The composition of claim 17, wherein the valency platform molecules individually comprise a core group and at least three arms wherein each arm comprises a terminus.

Claim 54 (Previously presented): The composition of claim 53, wherein the core group comprises the high molecular weight polyethylene oxide group.

Claim 55 (Previously presented): The composition of claim 53, wherein an arm comprises the high molecular weight polyethylene oxide group.

Claim 56 (Previously presented): The composition of claim 53, wherein the high molecular weight polyethylene oxide group is attached to the core or one of said arms.

Claim 57 (Canceled)

Claim 58 (Currently amended): The composition of claim 17, wherein the valency platform molecules prior to conjugation individually comprise at least three reactive conjugating groups selected from the group consisting of hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide, aldehyde, ketone, carboxylic acid halide, α -halocarbonyl, α,β -unsaturated carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea, hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide, α,β -unsaturated sulfone, aminoxy, semicarbazide, and β -aminothiol.

Claim 59 (Currently amended): The composition of claim 17, wherein the valency platform molecules prior to conjugation individually comprise at least 3 aminoxy groups.

Claim 60 (Previously presented): The composition of claim 17, wherein the valency platform molecules individually comprise at least 3 carbamate groups.

Claim 61 (Previously presented): A composition comprising chemically defined valency platform molecules, wherein the chemically defined valency platform molecules individually comprise a first and a second polyethylene oxide group, wherein the first and the second polyethylene oxide groups each have a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 18,000 Da, and wherein said valency platform molecules have a polydispersity less than 1.2.

Claim 62 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 20,000 Da.

Claim 63 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 22,000 Da.

Claim 64 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 30,000 Da.

Claim 65 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 40,000 Da.

Claim 66 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 35,200 Da.

Claim 67 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 39,600 Da.

Claim 68 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 44,000 Da.

Claim 69 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is 22,900-26,400 Da.

Claim 70 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is 24,200-30,800 Da.

Claim 71 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is 26,400-44,000 Da.

Claim 72 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is 26,400-39,600 Da.

Claim 73 (Previously presented): The composition of claim 61, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is 26,400-35,200 Da.

Claim 74 (Previously presented): The composition of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of greater than about 10,000 Da.

Claim 75 (Previously presented): The composition of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 5,000-10,000 Da.

Claim 76 (Previously presented): The composition of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 8,000-20,000 Da.

Claim 77 (Previously presented): The composition of claim 61, wherein the first and the second polyethylene oxide groups each have a molecular weight of about 10,000-20,000 Da.

Claim 78 (Previously presented): The composition of claim 61, wherein the chemically defined valency platform molecules individually comprise a third and a fourth polyethylene oxide group.

Claim 79 (Previously presented): The composition of claim 78, wherein the first, second, third, and fourth polyethylene oxide groups each have a molecular weight of about 8,000-20,000 Da.

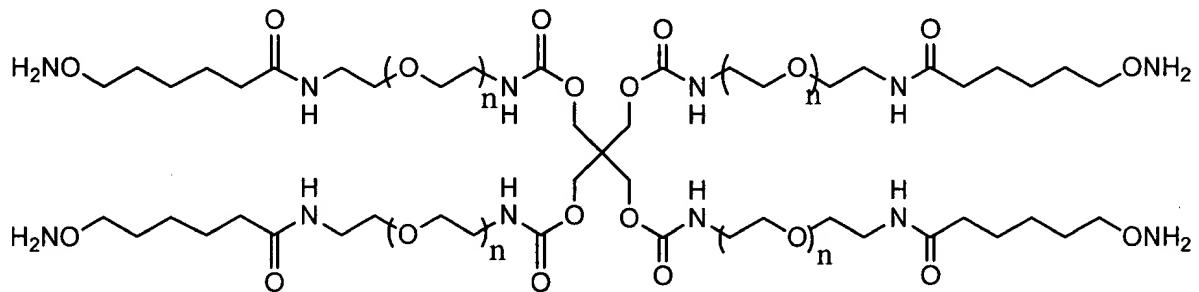
Claim 80 (Previously presented): The composition of claim 78, wherein the molecular weight of the first, second, third, and fourth polyethylene oxide groups in each valency platform molecule in combination is 26,400-44,000 Da.

Claim 81 (Currently amended): The composition of claim 96, wherein the biologically active molecules are β_2 GPI domain I polypeptides or analogs thereof that specifically [[binds]] bind to [[a]] β_2 GPI-dependent antiphospholipid antibody antibodies.

Claim 82 (Previously presented): The composition of claim 81, wherein the biologically active molecules are β_2 GPI domain I polypeptides.

Claim 83 (Previously presented): A composition comprising conjugates comprising biologically active molecules and the valency platform molecules of claim 80, wherein the biologically active molecules are β_2 GPI domain I polypeptides.

Claim 84 (Previously presented): A chemically defined valency platform molecule having the formula:



or an aminoxy protected form thereof; wherein the molecular weight of the polyethylene oxide groups in combination is 26,400-44,000 Da.

Claim 85 (Previously presented): A chemically defined valency platform molecule having the formula:



or an aminoxy protected form thereof;

wherein y is 2 to 16;

n is 1 to 32;

R_1 is H;

R_c is a hydrocarbyl group having from 1 to 200 carbon atoms;

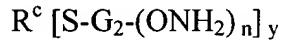
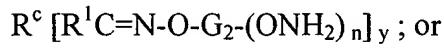
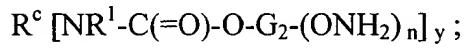
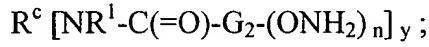
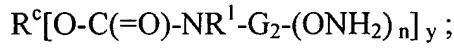
each G₂ independently comprises a polyethylene oxide group having a molecular weight of 44 to 22,000 Da;

wherein each G₂ further comprises an amide group;

with the proviso that the formula comprises at least a first and a second G₂ group, wherein the molecular weight of the polyethylene oxide groups in the first and the second G₂ groups are greater than about 5,000 Da; and

wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 86 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



or an aminoxy protected form thereof;

wherein:

y is 1 to 16;

n is 1 to 32;

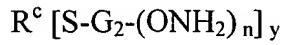
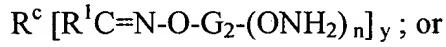
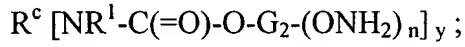
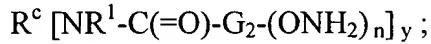
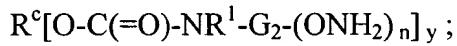
R¹ is H, alkyl, heteroalkyl, aryl, heteroaryl or G₂-(ONH₂)_n;

R^c is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups; and

G₂ is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups;

with the proviso that at least one of the R^c or G₂ groups comprises a high molecular weight polyethylene oxide group having a molecular weight of greater than about 18,000 Da.

Claim 87 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



or an aminoxy protected form thereof;

wherein:

y is 1 to 16;

n is 1 to 32;

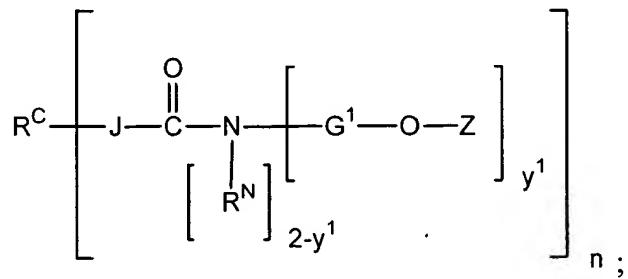
R^1 is H, alkyl, heteroalkyl, aryl, heteroaryl or $G_2-(ONH_2)_n$;

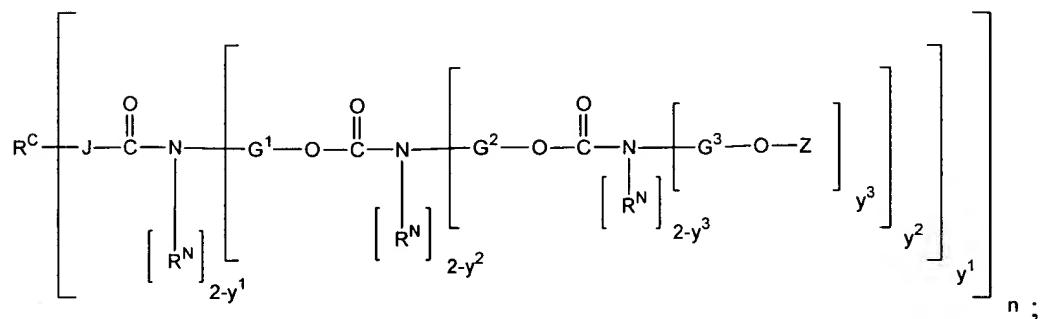
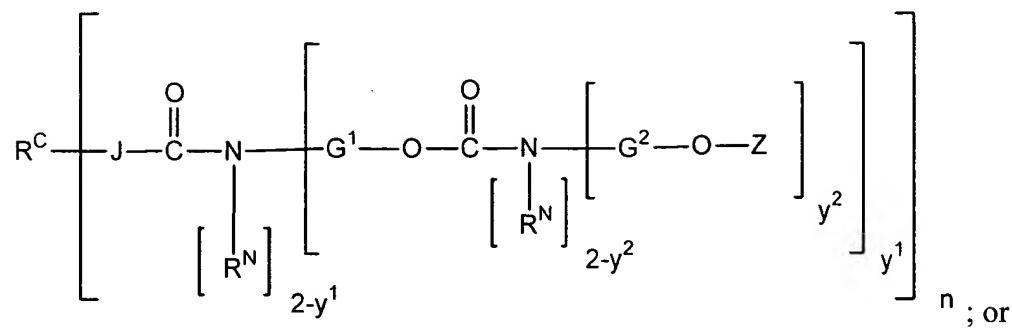
R^c is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups; and

G_2 is an organic moiety comprising atoms selected from the group consisting of H, C, N, O, P, Si and S atoms, and optionally comprising one or more polyethylene oxide groups;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 88 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently 1 or 2;

J independently denotes either an oxygen atom or a covalent bond;

R^C is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms; and

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^c optionally further comprises one or more polyethylene oxide groups;

each G¹, G², and G³ is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G¹, G², and G³ may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

-C(=O)NR^{AB}

wherein:

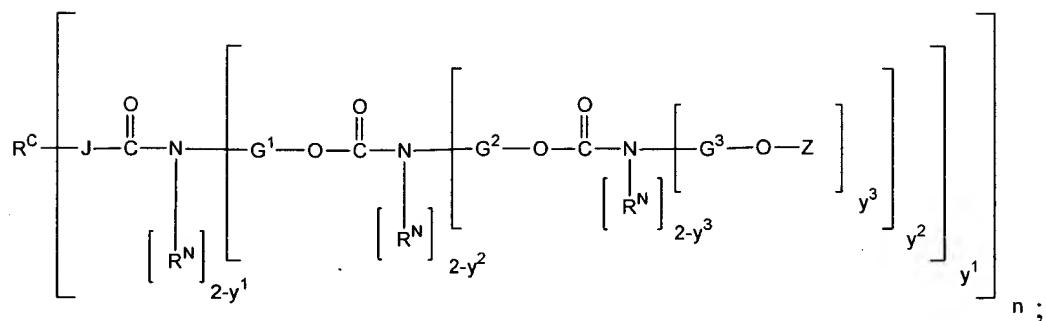
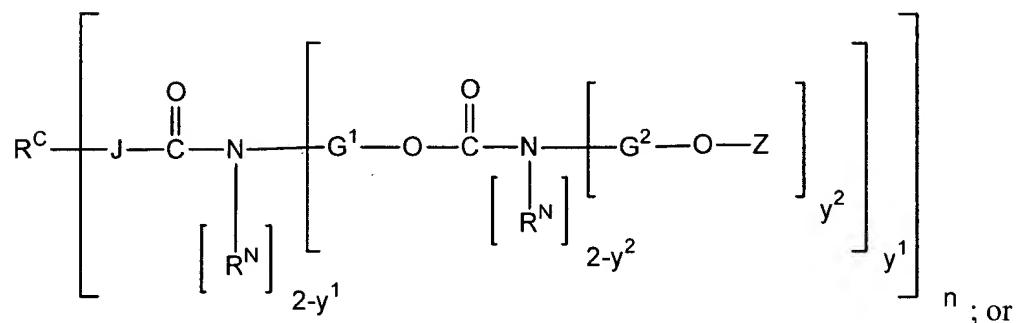
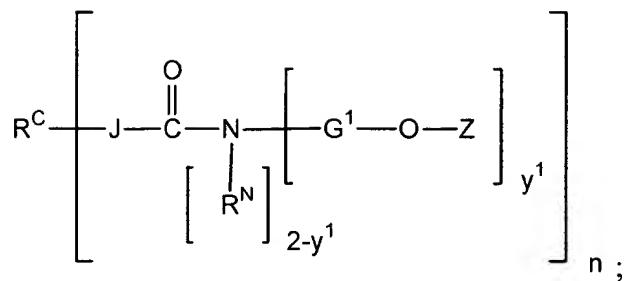
each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

each monovalent R^A and R^B and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

with the proviso that at least one of the R^c, G¹, G², or G³ groups comprises a high molecular weight polyethylene oxide group having a molecular weight of greater than about 18,000 Da.

Claim 89 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently 1 or 2;

J independently denotes either an oxygen atom or a covalent bond;

R^c is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms; and

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^c optionally further comprises one or more polyethylene oxide groups;

each G^1 , G^2 , and G^3 is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G^1 , G^2 , and G^3 may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;
alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;
aromatic groups having from 6 to 20 carbon atoms;
heteroaromatic groups having from 3 to 20 carbon atoms;
each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

-C(=O)NR^{AB}

wherein:

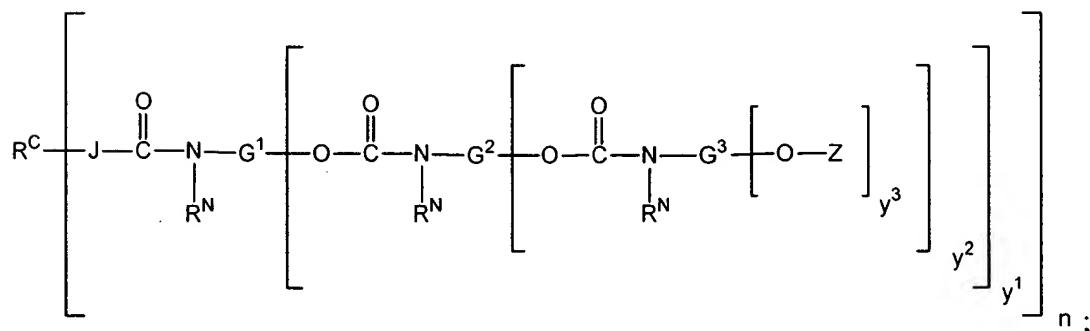
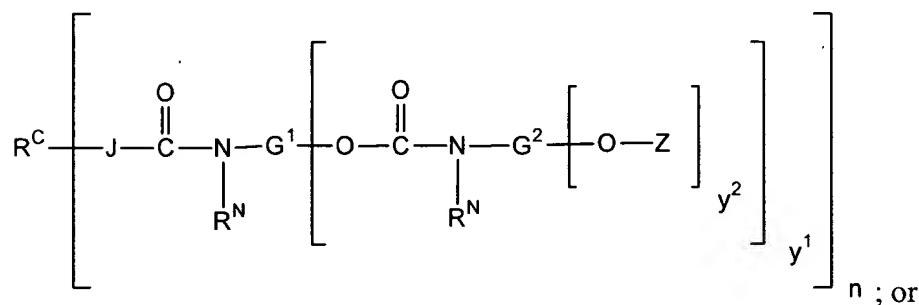
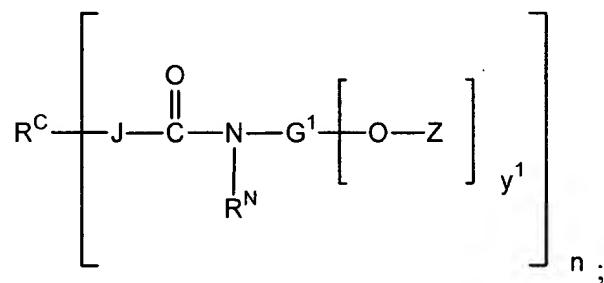
each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

each monovalent R^A and R^B and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 90 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



wherein:

n is an integer from 1 to 10;

y¹, y², and y³ are independently a positive integer from 1 to 10;

J independently denotes either an oxygen atom or a covalent bond;

R^c is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^c optionally further comprises one or more polyethylene oxide group;

each G¹, G², and G³ is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G¹, G², and G³ may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B

-C(=O)NR^{AB}

wherein:

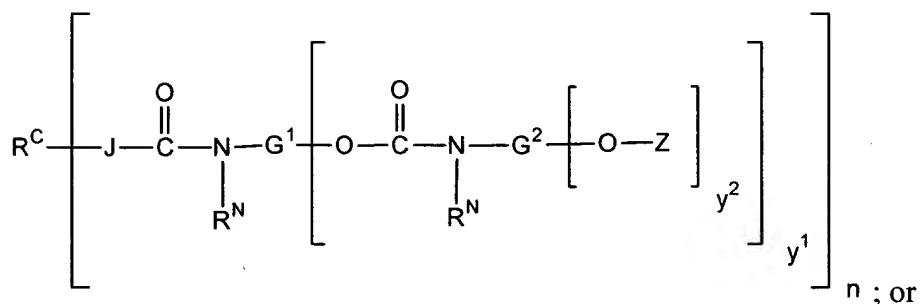
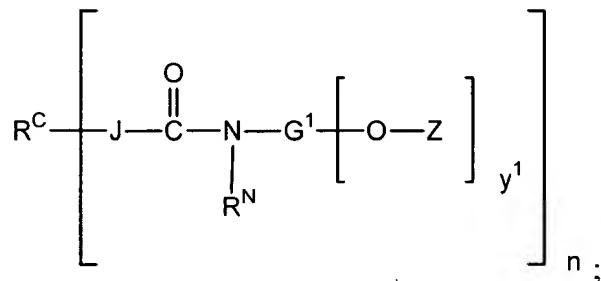
each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

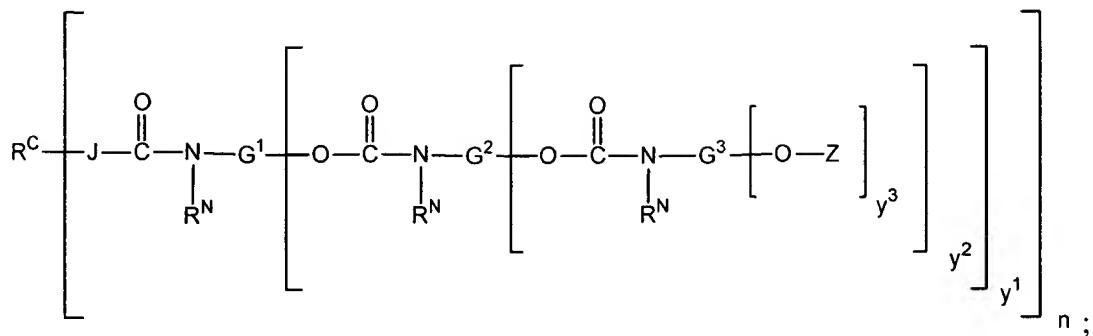
each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

each monovalent R^A and R^B and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

with the proviso that at least one of the R^c , G^1 , G^2 , or G^3 groups comprises a high molecular weight polyethylene oxide group having a molecular weight of greater than about 18,000 Da.

Claim 91 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:





wherein:

n is an integer from 1 to 10;

y^1 , y^2 , and y^3 are independently a positive integer from 1 to 10;

J independently denotes either an oxygen atom or a covalent bond;

R^C is selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, sulfur, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein R^C optionally further comprises one or more polyethylene oxide groups;

each G^1 , G^2 , and G^3 is independently selected from the group consisting of:

hydrocarbyl groups having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

organic groups consisting only of carbon, oxygen, nitrogen, and hydrogen atoms, and having from 1 to 20 carbon atoms;

and wherein each G¹, G², and G³ may independently further comprise one or more polyethylene oxide groups;

each R^N is independently selected from the group consisting of:

hydrogen;

linear or branched alkyl groups having from 1 to 15 carbon atoms;

alkyl groups comprising an alicyclic structure and having from 1 to 15 carbon atoms;

aromatic groups having from 6 to 20 carbon atoms;

heteroaromatic groups having from 3 to 20 carbon atoms;

each Z is independently selected from the group consisting of:

-H

-C(=O)OR^{CARB}

-C(=O)R^{ESTER}

-C(=O)NR^AR^B



wherein:

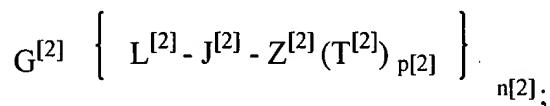
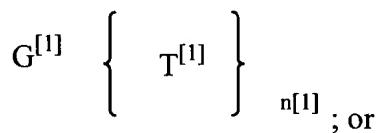
each R^{CARB} is independently an organic group comprising from 1 to about 20 carbon atoms;

each R^{ESTER} is independently an organic group comprising from 1 to about 20 carbon atoms;

each monovalent R^{A} and R^{B} and each divalent R^{AB} is independently H or an organic group comprising from 1 to 20 carbon atoms, and further comprising a reactive conjugating functional group;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 92 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



wherein

each of G^[1] and G^[2], if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein G^[1] and G^[2], if present, optionally further comprises one or more polyethylene oxide groups;

each T^[1] and each T^[2], if present, is independently chosen from the group NHR^{SUB}, C(=O)NHNHR^{SUB}, NHNHR^{SUB}, C(=O)OH, C(=O)OR^{ESTER}, C(=O)OC(=O)R^B, C(=O)X, S(=O)₂X, C(=NR^{SUB})OR^{SUB}, NCO, NCS, OC(=O)X, C(=O)OC(=NR^{SUB})NHR^{SUB}, C(=O)H, C(=O)R^B, SH, OH, C(=O)CH₂X, R^{ALK}X, S(=O)₂OR^{ALK}X, NR¹R² wherein R¹R² is -C(=O)CH=CHC(=O)-, C(=O)CR^B=CR^B₂, R^{ALK}-Hg-X, S(=O) CR^B=CR^B₂, and ONH₂;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each R^{ESTER} is independently N-succinimidyl, p-nitrophenyl, pentafluorophenyl, tetrafluorophenyl, pentachlorophenyl, 2,4,5-trichlorophenyl, 2,4-dinitrophenyl, cyanomethyl, 5-chloro,8-quinolone, 1-piperidine, or N-benzotriazole;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

each L^[2], if present, is independently chosen from the group O, NR^{SUB} and S;

each $J^{[2]}$, if present, is independently chosen from the group C(=O) and C(=S);

each $Z^{[2]}$, if present, is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, and forming attachment sites for at least $p^{[2]}$ functional groups, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Z^{[2]}$, if present, optionally further comprises one or more polyethylene oxide groups;

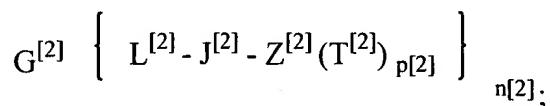
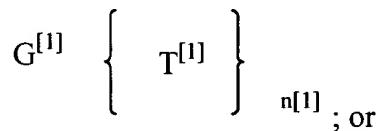
$n^{[1]}$, if present, is 1 to 32;

$n^{[2]}$, if present, is 1 to 32; and

$p^{[2]}$, if present, is 1 to 8; with the proviso that the product $n^{[2]} \times p^{[2]}$ be greater than 1 and less than 33;

with the proviso that at least one of the $G^{[1]}$, $G^{[2]}$, or $Z^{[2]}$ groups comprises a high molecular weight polyethylene oxide group having a molecular weight of greater than about 18,000 Da.

Claim 93 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



wherein

each of G^[1] and G^[2], if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein G^[1] and G^[2], if present, optionally further comprises one or more polyethylene oxide groups;

each T^[1] and each T^[2], if present, is independently chosen from the group NHR^{SUB}, C(=O)NHNHR^{SUB}, NHNHR^{SUB}, C(=O)OH, C(=O)OR^{ESTER}, C(=O)OC(=O)R^B, C(=O)X, S(=O)₂X, C(=NR^{SUB})OR^{SUB}, NCO, NCS, OC(=O)X, C(=O)OC(=NR^{SUB})NHR^{SUB}, C(=O)H, C(=O)R^B, SH, OH, C(=O)CH₂X, R^{ALK}X, S(=O)₂OR^{ALK}X, NR¹R² wherein R¹R² is -C(=O)CH=CHC(=O)-, C(=O)CR^B=CR^B₂, R^{ALK}-Hg-X, S(=O) CR^B=CR^B₂, and ONH₂;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (6-20C), or alkaryl (7-30C);

each R^{ESTER} is independently N-succinimidyl, p-nitrophenyl, pentafluorophenyl, tetrafluorophenyl, pentachlorophenyl, 2,4,5-trichlorophenyl, 2,4-dinitrophenyl, cyanomethyl, 5-chloro,8-quinolone, 1-piperidine, or N-benzotriazole;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

each L^[2], if present, is independently chosen from the group O, NR^{SUB} and S;

each $J^{[2]}$, if present, is independently chosen from the group C(=O) and C(=S);

each $Z^{[2]}$, if present, is independently a radical comprising 1-200 atoms selected from the group C, H, N, O, Si, P and S, and forming attachment sites for at least $p^{[2]}$ functional groups, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Z^{[2]}$, if present, optionally further comprises one or more polyethylene oxide groups;

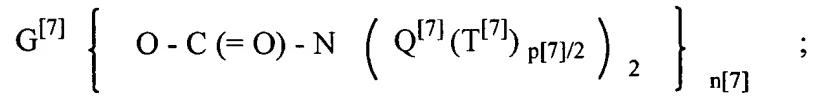
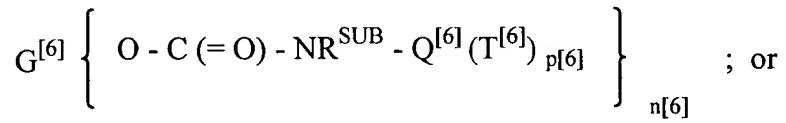
$n^{[1]}$, if present, is 1 to 32;

$n^{[2]}$, if present, is 1 to 32;

$p^{[2]}$, if present, is 1 to 8; with the proviso that the product $n^{[2]} \times p^{[2]}$ be greater than 1 and less than 33;

with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 94 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



wherein

each of G^[6] and G^[7], if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein G^[6] and G^[7], if present, optionally further comprises one or more polyethylene oxide groups;

each T^[6] and each T^[7], if present, is independently chosen from the group NHR^{SUB}, C(=O)NHNHR^{SUB}, NHNHR^{SUB}, C(=O)OH, C(=O)OR^{ESTER}, C(=O)OC(=O)R^B, C(=O)X, S(=O)₂X, C(=NR^{SUB})OR^{SUB}, NCO, NCS, OC(=O)X, C(=O)OC(=NR^{SUB})NHR^{SUB}, C(=O)H, C(=O)R^B, SH, OH, C(=O)CH₂X, R^{ALK}X, S(=O)₂OR^{ALK}X, NR¹R² wherein R¹R² is -C(=O)CH=CHC(=O)-, C(=O)CR^B=CR^B₂, R^{ALK}-Hg-X, S(=O)CR^B=CR^B₂, and ONH₂;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each R^{ESTER} is independently N-hydroxysuccinimidyl, p-nitrophenoxy, or pentafluorophenoxy;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

$n^{[6]}$, if present, is 1 to 32;

$p^{[6]}$, if present, is 1 to 8;

with the proviso that the product $n^{[6]} \times p^{[6]}$ be greater than 1 and less than 33;

$n^{[7]}$, if present, is 1 to 32;

$p^{[7]}$, if present, is 1 to 8;

with the proviso that the product $n^{[7]} \times p^{[7]}$ be greater than 1 and less than 33;

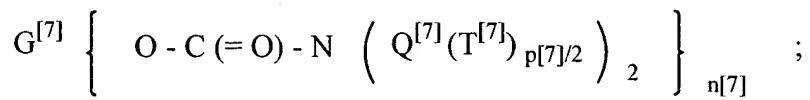
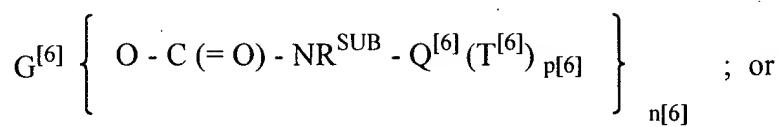
each $Q^{[6]}$ and each $Q^{[7]}$, if present, is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, and wherein each $Q^{[6]}$ and $Q^{[7]}$ moiety, if present, forms attachment sites for at least $p^{[6]}$ or $p^{[7]/2}$ functional groups, respectively, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein $Q^{[6]}$ and $Q^{[7]}$, if present, optionally further comprises one or more polyethylene oxide groups; and

wherein $p^{[7]/2}$ is an integer;

with the proviso that at least one of the $G^{[6]}$, $G^{[7]}$, $Q^{[6]}$, or $Q^{[7]}$ groups comprises a high molecular weight polyethylene oxide group having a molecular weight of greater than about 18,000 Da.

Claim 95 (Previously presented): A chemically defined valency platform molecule having the structure of one of the following formulae:



wherein

each of $G^{[6]}$ and $G^{[7]}$, if present, is independently a linear, branched or multiply-branched chain comprising 1-2,000 chain atoms selected from the group C, N, O, Si, P and S;

and wherein $G^{[6]}$ and $G^{[7]}$, if present, optionally further comprises one or more polyethylene oxide groups;

each $T^{[6]}$ and each $T^{[7]}$, if present, is independently chosen from the group NHR^{SUB} , $C(=O)NHNHR^{SUB}$, $NHNHR^{SUB}$, $C(=O)OH$, $C(=O)OR^{ESTER}$, $C(=O)OC(=O)R^B$, $C(=O)X$, $S(=O)_2X$, $C(=NR^{SUB})OR^{SUB}$, NCO , NCS , $OC(=O)X$, $C(=O)OC(=NR^{SUB})NHR^{SUB}$, $C(=O)H$, $C(=O)R^B$, SH , OH , $C(=O)CH_2X$, $R^{ALK}X$, $S(=O)_2OR^{ALK}X$, NR^1R^2 wherein R^1R^2 is $-C(=O)CH=CHC(=O)-$, $C(=O)CR^B=CR^B_2$, $R^{ALK}-Hg-X$, $S(=O)CR^B=CR^B_2$, and ONH_2 ;

wherein

each X is independently a halogen of atomic number greater than 16 and less than 54 or other leaving group;

each R^{ALK} is independently a linear, branched, or cyclic alkyl (1-20C) group;

each R^{SUB} is independently H, linear, branched, or cyclic alkyl (1-20C), aryl (1-20C), or alkaryl (1-30C);

each R^{ESTER} is independently N-hydroxysuccinimidyl, p-nitrophenoxy, or pentafluorophenoxy;

each R^B is independently a radical comprising 1-50 atoms selected from the group C, H, N, O, Si, P and S;

n^[6], if present, is 1 to 32;

p^[6], if present, is 1 to 8;

with the proviso that the product n^[6] x p^[6] be greater than 1 and less than 33;

n^[7], if present, is 1 to 32;

p^[7], if present, is 1 to 8;

with the proviso that the product n^[7] x p^[7] be greater than 1 and less than 33;

each Q^[6] and each Q^[7], if present, is independently a radical comprising 1-100 atoms selected from the group C, H, N, O, Si, P and S, , and wherein each Q^[6] and Q^[7] moiety, if present, forms attachment sites for at least p^[6] or p^{[7]/2} functional groups, respectively, wherein the attachment sites are alkyl, alkenyl, or aromatic carbon atoms;

and wherein Q^[6] and Q^[7], if present, optionally further comprises one or more polyethylene oxide groups; and

wherein p^{[7]/2} is an integer;

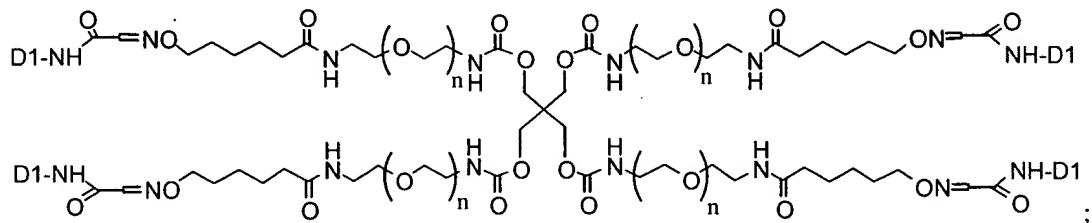
with the proviso that the valency platform molecule comprises at least 2 polyethylene oxide groups each having a molecular weight of greater than about 5,000 Da, and wherein the total of the molecular weights of all polyethylene oxide groups in the valency platform molecule in combination is greater than about 18,000 Da.

Claim 96 (Previously presented): A composition comprising conjugates comprising biologically active molecules and the valency platform molecules according to claim 61.

Claim 97 (Currently amended): The composition of claim 96, wherein the biologically active molecules are selected from the group consisting of ~~a polysaccharide, a polypeptide, a nucleic acid, and a lipid~~ polysaccharides, polypeptides, nucleic acids, and lipids.

Claim 98 (Previously presented): The composition of claim 96, wherein the biologically active molecules are polypeptides.

Claim 99 (Previously presented): A conjugate of a valency platform molecule and a biologically active molecule, having the formula:



wherein the molecular weight of the polyethylene oxide groups in combination is 26,400-44,000 Da; and

wherein D1 in said structures is a polypeptide consisting of amino acids No. 2-63 of SEQ ID NO: 2.

Claim 100 (Currently amended): A pharmaceutically acceptable composition comprising conjugates comprising biologically active molecules and the valency platform molecules according to any one of claims 84-95 and a pharmaceutically acceptable carrier.

Claim 101 (Canceled)

Claim 102 (Previously presented): The composition of claim 20, wherein the biologically active molecules comprise said nucleic acid.

Claim 103 (Previously presented): The composition of claim 21, wherein the biologically active molecules are β2GPI domain 1 polypeptides.

Claim 104 (Previously presented): A pharmaceutically acceptable composition comprising the composition of claim 19 and a pharmaceutically acceptable carrier.

Claim 105 (Previously presented): A pharmaceutically acceptable composition comprising the composition of claim 20 and a pharmaceutically acceptable carrier.

Claim 106 (Previously presented): A pharmaceutically acceptable composition comprising the composition of claim 21 and a pharmaceutically acceptable carrier.

Claim 107 (Previously presented): A pharmaceutically acceptable composition comprising the composition of claim 22 and a pharmaceutically acceptable carrier.

Claim 108 (Previously presented): A method of making the conjugates according to claim 17 or 96, comprising covalently bonding the biologically active molecules to the valency platform molecules to form conjugates.

Claim 109 (Previously presented): A method for treating an antibody mediated disease, comprising administering to the individual an effective amount of the composition according to claim 17 or 96.

Claim 110 (New): The composition of claim 1, wherein said valency platform molecules have a polydispersity less than 1.07.

Claim 111 (New): The composition of claim 9, wherein the valency platform molecules individually comprise at least three carbamate groups and at least three aminoxy groups, wherein the aminoxy groups are protected.

Claim 112 (New): The composition of claim 111, wherein the high molecular weight polyethylene oxide group has a molecular weight greater than about 20,000 Daltons.

Claim 113 (New): The composition of claim 111, wherein the high molecular weight polyethylene oxide group has a molecular weight greater than about 22,000 Daltons.

Claim 114 (New): The composition of claim 14, wherein the valency platform molecules individually comprise at least three amine reactive conjugating functional groups.

Claim 115 (New): The composition of claim 15, wherein the aminoxy groups are protected.

Claim 116 (New): The composition of claim 17, wherein the valency platform molecules have a polydispersity less than 1.07.

Claim 117 (New): The composition of claim 18, wherein the biologically active molecules are polypeptides.

Claim 118 (New): The composition of claim 18, wherein the biologically active molecules are nucleic acids.

Claim 119 (New): The composition of claim 53, wherein the valency platform molecules individually comprise at least three carbamate groups, and wherein the valency platform molecules prior to conjugation individually comprise at least 3 aminoxy groups.

Claim 120 (New): The composition of claim 119, wherein the biologically active molecules are β 2GPI domain 1 polypeptides.

Claim 121 (New): The composition of claim 119, wherein the biologically active molecules comprise a nucleic acid which specifically binds to an anti-double stranded DNA antibody.

Claim 122 (New): The composition of claim 119, wherein the high molecular weight polyethylene oxide group has a molecular weight of at least about 22,000 Daltons.

Claim 123 (New): The composition of claim 122, wherein the biologically active molecules are β 2GPI domain 1 polypeptides.

Claim 124 (New): The composition of claim 122, wherein the biologically active molecules comprise a nucleic acid which specifically binds to an anti-double stranded DNA antibody.

Claim 125 (New): The composition of claim 58, wherein the valency platform molecules prior to conjugation individually comprise at least three amine reactive conjugating functional groups.

Claim 126 (New): A composition comprising conjugates according to claim 25, wherein the valency platform molecules have a polydispersity less than 1.2.

Claim 127 (New): The conjugate of claim 29, wherein the core group comprises the high molecular weight polyethylene oxide group.

Claim 128 (New): The conjugate of claim 29, wherein an arm comprises the high molecular weight polyethylene oxide group.

Claim 129 (New): The composition of claim 61, wherein the valency platform molecules individually comprise a core group and at least three arms wherein each arm comprises a terminus.

Claim 130 (New): The composition of claim 129, wherein the core group comprises at least one of the first and second polyethylene oxide groups.

Claim 131 (New): The composition of claim 129, wherein an arm comprises at least one of the first and second polyethylene oxide groups.

Claim 132 (New): The composition of claim 129, wherein at least one of the first and second polyethylene oxide groups is attached to the core or one of said arms.

Claim 133 (New): The composition of claim 129, wherein the valency platform molecules individually comprise at least three carbamate groups and at least three aminoxy groups, wherein the aminoxy groups are protected.

Claim 134 (New): The composition of claim 133, wherein the total of the molecular weights of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 20,000 Daltons.

Claim 135 (New): The composition of claim 133, wherein the total of the molecular weights of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 22,000 Daltons.

Claim 136 (New): The composition of claim 133, wherein all polyethylene oxide groups in each valency platform molecule are in the arms.

Claim 137 (New): The composition of claim 61, wherein the valency platform molecules individually comprise at least three reactive conjugating groups selected from the group consisting of hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide,

aldehyde, ketone, carboxylic acid halide, α -halocarbonyl, α,β -unsaturated carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea, hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide, α,β -unsaturated sulfone, aminoxy, semicarbazide, and β -aminothiol.

Claim 138 (New): The composition of claim 137, wherein the valency platform molecules individually comprise at least three amine reactive conjugating functional groups.

Claim 139 (New): The composition of claim 61, wherein the valency platform molecules individually comprise at least 3 aminoxy groups.

Claim 140 (New): The composition of claim 139, wherein the aminoxy groups are protected.

Claim 141 (New): The composition of claim 61, wherein the valency platform molecules individually comprise at least 3 carbamate groups.

Claim 142 (New): The composition of claim 61, wherein the valency platform molecules have a polydispersity less than 1.07.

Claim 143 (New): The composition of claim 78, wherein the valency platform molecules individually comprise a core group and four arms, wherein each arm comprises one of said first, second, third, and fourth polyethylene glycol groups.

Claim 144 (New): The composition of claim 96, wherein the biologically active molecules are nucleic acids.

Claim 145 (New): The composition of claim 96, wherein the biologically active molecules comprise a nucleic acid which specifically binds to an anti-double stranded DNA antibody.

Claim 146 (New): A pharmaceutically acceptable composition comprising the composition of claim 145 and a pharmaceutically acceptable carrier.

Claim 147 (New): The composition of claim 96, wherein the conjugates are B cell toleragens.

Claim 148 (New): A pharmaceutically acceptable composition comprising the composition of claim 147 and a pharmaceutically acceptable carrier.

Claim 149 (New): The composition of claim 96, wherein the biologically active molecules are α Gal epitopes.

Claim 150 (New): The composition of claim 96, wherein the valency platform molecules individually comprise a core group and at least three arms wherein each arm comprises a terminus.

Claim 151 (New): The composition of claim 150, wherein the core group comprises at least one of the first and second polyethylene oxide groups.

Claim 152 (New): The composition of claim 150, wherein an arm comprises at least one of the polyethylene oxide groups.

Claim 153 (New): The composition of claim 150, wherein at least one of the first and second polyethylene oxide groups is attached to the core or one of said arms.

Claim 154 (New): The composition of claim 150, wherein the valency platform molecules individually comprise at least three carbamate groups, and wherein the valency platform molecules prior to conjugation individually comprise at least 3 aminoxy groups.

Claim 155 (New): The composition of claim 154, wherein the biologically active molecules are β 2GPI domain 1 polypeptides.

Claim 156 (New): The composition of claim 154, wherein the biologically active molecules comprise a nucleic acid which specifically binds to an anti-double stranded DNA antibody.

Claim 157 (New): The composition of claim 154, wherein the total of the molecular weights of all polyethylene oxide groups in each valency platform molecule in combination is greater than about 22,000 Daltons.

Claim 158 (New): The composition of claim 157, wherein the biologically active molecules are β 2GPI domain 1 polypeptides.

Claim 159 (New): The composition of claim 157, wherein the biologically active molecules comprise a nucleic acid which specifically binds to an anti-double stranded DNA antibody.

Claim 160 (New): The composition of claim 154, wherein the molecular weight of all polyethylene oxide groups in each valency platform molecule in combination is 26,400-44,000 Da.

Claim 161 (New): The composition of claim 160, wherein the biologically active molecules are β 2GPI domain 1 polypeptides.

Claim 162 (New): The composition of claim 160, wherein the biologically active molecules comprise a nucleic acid which specifically binds to an anti-double stranded DNA antibody.

Claim 163 (New): The composition of claim 96, wherein the valency platform molecules prior to conjugation individually comprise at least three reactive conjugating groups selected from the group consisting of hydroxyl, thiol, isocyanate, isothiocyanate, amine, alkyl halide, alkylmercurial halide, aldehyde, ketone, carboxylic acid halide, α -halocarbonyl, α,β -unsaturated carbonyl, haloformate ester, carboxylic acid, carboxylic ester, carboxylic anhydride, O-acyl isourea,

hydrazide, maleimide, imidate ester, sulfonate ester, sulfonyl halide, α,β -unsaturated sulfone, aminoxy, semicarbazide, and β -aminothiol.

Claim 164 (New): The composition of claim 163, wherein the valency platform molecules prior to conjugation individually comprise at least three amine reactive conjugating functional groups.

Claim 165 (New): The composition of claim 96, wherein the valency platform molecules prior to conjugation individually comprise at least 3 aminoxy groups.

Claim 166 (New): The composition of claim 96, wherein the valency platform molecules individually comprise at least 3 carbamate groups.

Claim 167 (New): The composition of claim 96, wherein the valency platform molecules have a polydispersity less than 1.07.

Claim 168 (New): A pharmaceutically acceptable composition comprising the composition of claim 82 and a pharmaceutically acceptable carrier.

Claim 169 (New): The composition of claim 82, wherein the conjugates are effective for the treatment of antibody mediated thrombosis.

Claim 170 (New): A pharmaceutically acceptable composition comprising the composition of claim 169 and a pharmaceutically acceptable carrier.

Claim 171 (New): The composition according to claim 100, wherein the biologically active molecules are polypeptides.

Claim 172 (New): The composition according to claim 100, wherein the biologically active molecules are nucleic acids.

Claim 173 (New): A method for treating an antibody mediated disease, comprising administering to the individual an effective amount of the composition according to claim 99.